BIOGRAPHICAL SKETCH

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NAME: Pamela Gehron Robey

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Senior Investigator

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Susquehanna University, Selinsgrove, PA	B.A.	1974	Biology
Catholic University of America, Washington, D.C.	M.S.	1977	Biochemistry
Catholic University of America, Washington, D.C.	Ph.D.	1979	Cell Biology

A. Personal Statement

Since 1982, my work has focused on determination of the biological nature of osteogenic cells and their precursors (skeletal stem cells, also known as bone marrow-derived “mesenchymal stem cells”), with a particular emphasis on the role that they play in disease, and how they can be used in tissue engineering and regenerative medicine. I have extensive expertise in chondrogenic, osteogenic and adipogenic differentiation assays, and in animal models of bone formation, such as the generation of subcutaneous ectopic ossicles. vivo.

B. Positions and Honors

1974-1979	Biologist, Connective Tissue Section, Laboratory of Developmental Biology and Anomalies, National Institute of Dental Research, National Institutes of Health
1978	Sigma Xi Research Award
1979-1980	Individual National Research Service Awardee, Genetics and Biochemistry Branch, National Institute of Arthritis, Metabolism and Digestive Diseases, National Institutes of Health
1981-1983	Staff Fellow, Retinal and Ocular Connective Tissue Diseases Section, Clinical Branch, National Eye Institute, National Institutes of Health
1983-1987	Senior Staff Fellow, Bone Research Branch, NIDR, NIH
1985	Norwich-Eaton Young Investigator, American Society for Bone & Mineral Research Award
1987-1992	Research Biologist, Bone Research Branch, NIDR, NIH
1992-1997	Chief, Skeletal Biology Section, Bone Research Branch, NIDR, NIH
1993	Fuller Albright Award, American Society for Bone and Mineral Research
1994-1997	Chief, Bone Research Branch, NIDR, NIH
1994	NIH Group Merit Award
1997-2016	Chief, Craniofacial and Skeletal Diseases Branch, NIDCR, NHI
1997-Present	Chief, Skeletal Biology Section, CSDB, NIDCR, NIH
1998	NIH Director’s Award
1-9/2004	Acting Scientific Director, NIDCR, NIH
10/2004-2/2005	Acting Deputy Scientific Director, NIDCR, NIH
2004-2013	Chief, Matrix Metalloproteinase Section, CSDB, NIDCR, NIH
2005	NIH Group Merit Award
2008-2014	Co-Coordinator, NIH Bone Marrow Stromal Cell Transplantation Center
2009	IADR Isaac Shour Distinguished Scientist Award

2010-Present	Acting Director, NIH Stem Cell Unit
2010	NIH Director's Award
2012	NIH Clinical Director's Award
2014	NHLBI Director's Translational Research Award
2015	FNIDCR Outstanding NIDCR Career Research Award

C. Contribution to Science

1. Characterization of skeletal stem cells/bone marrow stromal cells (also known as "mesenchymal stem cells")

It has been long known from the pioneering work of Friedenstein and Owen that bone marrow contains a non-hematopoietic, fibroblastic bone marrow stromal cells (BMSCs) that are able to recreate cartilage, bone, hematopoiesis-supportive stroma and marrow adipocytes. These skeletal stem cells (SSCs) reside on the abluminal surfaces of bone marrow sinusoids and are pericytes. However, by clonal analysis and in vivo transplantation assay, the gold stand by which to assess differentiation, that not all pericytes are multipotent. We continue to work on ways to distinguish multipotent SSCs from more committed BMSCs.

1. Bianco P, Riminucci M, Gronthos S, **Robey PG** 2001 Bone marrow stromal stem cells: nature, biology, and potential applications. Stem Cells 19(3):180-92.
2. Bianco P*, **Robey PG***, Simmons PJ* 2008 Mesenchymal stem cells: revisiting history, concepts, and assays. Cell Stem Cell 2(4)**:**313-9. *These authors contributed equally.
3. Sworder BJ, Yoshizawa S, Mishra PJ, Cherman N, Kuznetsov SA, Merlino G, Balakumaran A, **Robey PG** 2015Molecular profile of clonal strains of human skeletal stem/progenitor cells with different potencies. Stem Cell Res 14:297-306.
4. Bianco P, **Robey PG** 2015 Skeletal stem cells. Development **142**:1023-1027
5. Sacchetti B, Funari A, Remoli C, Giannicola G, Kogler G, Liedtke S, Cossu G, Serafini M, Sampaolesis M, Tagliafico E, Tenedini E, Saggio I, **Robey PG**,* Riminucci M,* Bianco P No identical "mesenchymal stem cells" at different times and sites: Human committed progenitors of distinct origin and differentiation potential are incorporated as adventitial cells in microvessels. Stem Cell Reports 6:897-913. *Co-corresponding authors.

2. Determination of the role of skeletal stem cells/bone marrow stromal cells in disease

Based on the fact that SSCs/BMSCs are critical not only for new bone formation, but also for the formation and control of osteoclasts, SSCs/BMSCs are central mediators of skeletal homeostasis. We hypothesized that any mutation (intrinsic change) or change in their microenvironment (extrinsic change) would lead to a skeletal disorder. Proof of principle came from studies of fibrous dysplasia of bone, in which we demonstrated that mutated SSCs/BMSCs recreated a fibrous dysplastic lesion upon in vivo transplantation into immunocompromised mice. Due to the fact that SSCs/BMSCs are the only cell type found to support normal post-natal hematopoiesis, we also hypothesized that mutations in SSCs/BMSCs may also impact on hematopoiesis, such as in telomere biology diseases such as dyskeratosis congenita. SSCs/BMSCs along with in vivo transplantation assays represent a useful model in study the pathogenetic mechanisms in skeletal and perhaps in some hematopoietic diseases.

1. Bianco P, Kuznetsov SA, Riminucci M, Fisher LW, Spiegel AM, **Robey PG** 1998 Reproduction of human fibrous dysplasia of bone in immunocompromised mice by transplanted mosaics of normal and Gsalpha-mutated skeletal progenitor cells. J Clin Invest **101**(8)**:**1737-44.
2. Bianco P, Riminucci M, Majolagbe A, Kuznetsov SA, Collins MT, Mankani MH, Corsi A, Bone HG, Wientroub S, Spiegel AM, Fisher LW, **Robey PG** 2000 Mutations of the GNAS1 gene, stromal cell dysfunction, and osteomalacic changes in non-McCune-Albright fibrous dysplasia of bone. J Bone Miner Res 15(1)**:**120-8.
3. Kuznetsov SA, Cherman N, Riminucci M, Collins MT, **Robey PG**, Bianco P 2008 Age-dependent demise of GNAS-mutated skeletal stem cells and "normalization" of fibrous dysplasia of bone. J Bone Miner Res **23**(11)**:**1731-40.
4. Kuznetsov SA, Mankani MH, Bianco P, **Robey PG** 2009 Enumeration of the colony-forming units-fibroblast from mouse and human bone marrow in normal and pathological conditions. Stem Cell Res **2:**83-95.
5. Balakumaran A, Mishra PJ, Pawelczyk E, Yoshizawa S, Sworder BJ, Cherman N, Kuznetsov SA, Bianco P, Giri N, Savage SA, Merlino G, Dumitriu B, Dunbar CE, Young NS, Alter BP, **Robey PG** 2015 Bone

marrow skeletal progenitor cell defects in dyskeratosis congenital and telomere biology disorders. Blood **125**:793-802.

3. The use of stem cells in tissue engineering and regenerative medicine

Our in vivo transplantation studies have demonstrated that SSCs/BMSCs, when combined with an appropriate scaffold, have the ability to regenerate large segments of bone. We have been progressing towards translating this laboratory findings to clinical applications by refining the methods of ex vivo expansion, identifying osteo-conductive scaffolds, and preparation of GMP grade SSCs/BMSCs. In addition, we have been working on differentiating pluripotent stem cells into bona fide osteogenic cells, based on rigorous in vivo transplantation assays.

1. Mankani MH, Kuznetsov SA, Shannon B, Nalla RK, Ritchie RO, Qin Y, **Robey PG** 2006 Canine cranial reconstruction using autologous bone marrow stromal cells. Am J Pathol **168**(2)**:**542-50.
2. Mankani MH, Kuznetsov SA, Wolfe RM, Marshall GW, **Robey PG** 2006 In vivo bone formation by human bone marrow stromal cells: reconstruction of the mouse calvarium and mandible. Stem Cells **24**(9)**:**2140-9.
3. Mankani MH, Kuznetsov SA, Marshall GW, **Robey PG** 2008 Creation of new bone by the percutaneous injection of human bone marrow stromal cell and HA/TCP suspensions. Tissue Eng Part A **14**(12)**:**1949-58.
4. **Robey PG**, Kuznetsov SA, Ren J, Klein HG, Sabatino M, Stroncek DF 2015 Generation of clinical grade human bone marrow stromal cells for use in bone regeneration. Bone **70**:87-92.
5. Pillips MD,* Kuznetsov SA,* Cherman, N, Park K-Y, Chen, KG, McClendon BN, Hamilton RM, McKay R, Chenoweth, J, Mallon BM, **Robey PG** 2014 Directed differentiation of human induced pluripotent stem cells towards bone and cartilage: in vitro vs. in vivo assays. Stem Cells Trans Med 3:867-878. *Authors contributed equally.

D. Research Support

Current Research Support

Division of Intramural Research, NIDCR, Intramural Research Program, NIH, DHHS
ZIA DE000380 (1983-Present)
ZIA DE000676 (2004-Present)